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(12) # EUROPEAN PATENT APPLICATION

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The title of the invention has been amended (Guidelines for Examination in the EPO, A-III, 7.3).

(54) **Pharmaceutical compositions for topical use containing miocamycin.**

(57) The topical administration of the macrolide antibiotic miocamycin is proposed for the therapy of infections (caused by microbial flora sensitive to said antibiotic) of the skin and of the mucous membranes, this antibiotic being administered in suitable pharmaceutical forms such as ointment, globuli, ophthalmic ointment and mouthwash.

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Description

APPLICATION OF PHARMACEUTICAL FORMS FOR TOPICAL USE CONTAINING MIOCAMYCIN FOR THE THERAPY OF INFECTIONS CAUSED BY GERMS SENSITIVE TO SAID MIOCAMYCIN

The invention relates to the application of pharmaceutical forms based on miocamycin which are suitable for topical administration and which are effective in the therapy of infections of the skin and of the mucous membranes (conjunctival, oropharyngeal, and vulvo-vaginal-cervical) caused by germs sensitive to miocamycin.

The invention also relates to a method for the topical therapy of said infections. The antibiotic therapy of bacterial infections of the skin and of the mucous membranes, as well as those dermatological disorders in which a microbial etiological aspect is involved (for example, acne), makes use, depending upon the particular cases involved, not only of the systemic administration route but also - and on occasions exclusively - of the topical administration route. Various chemo-antibiotics such as tetracyclines, aminoglycosides, chloramphenicol, etc are, in fact, widely used via the topical route.

Miocamycin, a macrolide antibiotic with a spectrum of action such as to justify the use thereof in the infections set forth above (Yoshida et al., Jap. J. Antibiotics 135, 1462, 1982), although representing, as compared with other pharmaceutical products, an advantageous alternative both on account of the high degree of efficacy and on account of the excellent tolerability, has, to date, never been used for topical administration in the case of the abovementioned disorders.

The pharmaceutical forms of miocamycin suitable for topic.al administration, which represent a novel means for the administration of said miocamycin and which consist of: ointment, gel, globuli, ophthalmic ointment, mouthwash and other equivalent forms, form part of the present invention.

Non-limiting examples of the formulation of various pharmaceutical forms for topical administration are given herein below:

Example 1

An ointment having the following composition, related to 100 g:
Miocamycin from 1 to 5 g
Ethylcellulose from 0.08 to 0.4 g
Non-ionic surfactants from 3 to 7 g
Aliphatic mixed esters from 50 to 80 g
Glycerides of saturated fatty acids from 5 to 15 g
Preservatives from 0.05 to 0.2 g

Example 2

The pharmaceutical form is a gel and consists in a suitable bottle containing the excipient and provided with a reservoir cap containing the active principle to be combined with the excipient at the time of use. This is due to the poor stability of the active principle over a long period of time in the presence of water; the gel thickens on being administered to the tissues at body temperature.

The composition is the following, related to 100 g:
Content of the bottle:
Hydroxypropylmethylcellulose from 0.5 to 3 g
Poloxamers and/or poloxamines from 5 to 50 g
Preservatives from 0.05 to 0.2 g
Buffering substances q.s. at pH 7 - 7.5
Water q.s. to 100 g
Content of the reservoir cap:
Miocamycin from 1 to 5 g
Ethylcellulose from 0.08 to 0.4 g

Example 3

Globuli having the following unit composition:
Miocamycin from 0.25 to 0.8 g
Ethylcellulose from 0.02 to 0.07 g
Non-ionic surfactants from 0.05 to 0.15 g
Polyethylene glycols from 3 to 6 g
Propylene glycol from 0 to 2 g

Example 4

Globuli having the following unit composition:
Miocamycin from 0.25 to 0.8 g
Ethylcellulose from 0.02 to 0.07 g
Semisynthetic glycerides of saturated fatty acids from 3 to 6 g

Example 5

Mouthwash consisting of granules in a single-dose package, to be suspended in water at the time of use, and having the following unit composition:
Miocamycin from 0.3 to 0.9 g
Ethylcellulose from 0.024 to 0.08 g
Hydroxypropylmethylcellulose from 0.15 to 0.3 g
Mannitol from 1.5 to 4 g
Flavorings from 0.05 to 0.15 g
Dimethicone from 0.0005 to 0.001 g
Non-ionic surfactants from 0.0005 to 0.001 g
Synthetic sweetener from 0.005 to 0.05 g

Example 6

Ophthalmic ointment having the following composition per 100 g:
Miocamycin from 1 to 10 g
Ethylcellulose from 0.08 to 0.8 g
Vegetable oils from 20 to 30 g
Solid paraffin from 40 to 60 g
Non-ionic surfactants from 0.5 to 5 g
Polyoxyethylenated oleic glycerides from 5 to 10 g
Preservatives from 0.05 to 0.2 g

Claims

1. Pharmaceutical forms containing miocamycin for topical administration, to be used in infections of the skin and of the mucous membranes (ointment, gel, globuli, ophthalmic ointment, mouthwash and the like).

2. Use of the pharmaceutical forms as claimed in claim 1, for the therapy of infections of the skin and of the mucous membranes (conjunctival, oropharyngeal, and vulvo-vaginal-cervical).

3. Compositions of pharmaceutical forms for topical administration containing mikamycin.

4. The composition as claimed in claim 3 in ointment, having a formulation as follows, related to 100 g:
Miocamycin from 1 to 5 g
Ethylcellulose from 0.08 to 0.4 g
Non-ionic surfactants from 3 to 7 g
Aliphatic mixed esters from 50 to 80 g
Glycerides of saturated fatty acids from 5 to 15 g
Preservatives from 0.05 to 0.2 g

5. The composition as claimed in claim 3, having a formulation as follows, related to 100 g, in the pharmaceutical form of a gel, consisting in a suitable bottle containing the excipient and provided with a reservoir cap containing the active principle to be combined with the excipient at the time of use, on account of the poor stability of the active principle over a long period of time in the presence of water:
Content of the bottle:
Hydroxypropylmethylcellulose from 0.5 to 3 g
Poloxamers and/or poloxamines from 5 to 50 g
Preservatives from 0.05 to 0.2 g
Buffering substances q.s. at pH 7 - 7.5
Water q.s. to 100 g
Content of the reservoir cap:
Miocamycin from 1 to 5 g
Ethylcellulose from 0.08 to 0.4 g

6. The composition as claimed in claim 3, in the form of globuli having the following unit formulation:
Miocamycin from 0.25 to 0.8 g
Ethylcellulose from 0.02 to 0.07 g
Non-ionic surfactants from 0.05 to 0.15 g
Polyethylene glycols from 3 to 6 g
Propylene glycol from 0 to 2 g

7. The composition as claimed in claim 3, in the form of globuli having the following unit formulation:
Miocamycin from 0.25 to 0.8 g
Ethylcellulose from 0.02 to 0.07 g Semisynthetic glycerides of saturated fatty acids from 3 to 6 g

8. The composition as claimed in claim 3, in the form of mouthwash, granules in a single-dose packet, to be suspended in water at the time of use, having the following unit formulation:
Miocamycin from 0.3 to 0.9 g
Ethylcellulose from 0.024 to 0.08 g
Hydroxypropylmethylcellulose from 0.15 to 0.3 g
Mannitol from 1.5 to 4 g
Flavorings from 0.05 to 0.15 g
Dimethicone from 0.0005 to 0.001 g
Non-ionic surfactants from 0.0005 to 0.001 g
Synthetic sweetener from 0.005 to 0.05 g

9. The composition as claimed in claim 3, in the form of ophthalmic ointment having the following formulation per 100 g:
Miocamycin from 1 to 10 g
Ethylcellulose from 0.08 to 0.8 g
Vegetable oils from 20 to 30
Solid paraffin from 40 to 60 g
Non-ionic surfactants from 0.5 to 5 g
Polyoxyethylenated oleic glycerides from 5 to 10 g
Preservatives from 0.05 to 0.2 g

10. A method for the therapy of infections of the skin and of the mucous membranes, using the compositions as claimed in the preceding claims.

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PARTIAL EUROPEAN SEARCH REPORT

which under Rule 45 of the European Patent Convention shall be considered, for the purposes of subsequent proceedings, as the European search report

Application number

EP 88 83 0287

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.4)
A	GB-A-2 132 086 (TOYO JOZO CO. LTD) * Claims 1-22 * --		A 61 K 31/71 A 61 K 47/00
A	EP-A-0 135 617 (MEPHA AG) * Claims 1-9 * --		
A	US-A-4 335 115 (E.D. THOMPSON et al.) * Claims 1,2 * ----------		

TECHNICAL FIELDS SEARCHED (Int. Cl.4)

A 61 K

INCOMPLETE SEARCH

The Search Division considers that the present European patent application does not comply with the provisions of the European Patent Convention to such an extent that it is not possible to carry out a meaningful search into the state of the art on the basis of some of the claims.

Claims searched completely: 1,3-9

Claims searched incompletely:

Claims not searched: 2,10

Reason for the limitation of the search:

Method for treatment of the human or animal body by surgery or therapy (see art. 52(4) of the European Patent Convention).

Place of search	Date of completion of the search	Examiner
The Hague	28-09-1988	TZSCHOPPE

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

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